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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/398,897	09/20/1999	RENJI YANG	0109015/016	1629

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/398,897	Yang et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jan 22, 2002* .

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1, 4, 5, 12, 15, and 16* is/are pending in the application.

4a) Of the above, claim(s) ______ is/are withdrawn from consideration.

5) [ ] Claim(s) ______ is/are allowed.

6) [X] Claim(s) *1, 4, 5, 12, 15, and 16* is/are rejected.

7) [ ] Claim(s) ______ is/are objected to.

8) [ ] Claims ______ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on ______ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on ______ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. ______ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *2 & 7*

RCH 11/14/01

18) [ ] Interview Summary (PTO-413) Paper No(s). ______

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

DETAILED ACTION

Response to Amendment

1. The amendment filed 01/22/02 has been entered.

2. The rejections of claims 1-5 & 12-16 under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling for lack of critical or essential elements is withdrawn due to either the cancellation or amendment of the claims, and due to the Declaration under 37 CFR 1.132 filed 1/22/02 establishing that steroid hormone receptor ligand binding domains and c-myc constructs are structurally well known in the art at the time of filing the instant application.

3. The rejections of claims 1-5 & 12-16 under 35 U.S.C. 112, second paragraph are withdrawn due to the cancellation or amendment of the claims.

4. Applicant's arguments filed 01/22/02 have been fully considered but they are not deemed to be persuasive.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1, 4-5, 12 & 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakafuka et al (IDS Ref #26), in view of Weiss et al. (U.S. Patent 5,851,832; IDS Ref #2).

Nakafuka et al teach a method of producing stable mammalian neural precursor cells *in vitro* comprising preparing cultures of E12 embryonic rat neuroepithelial/neural precursor cells in Dulbecco's modified Eagle's medium with serum that reasonably contains mitogens, such as α FGF, bFGF, EGF and/or TGFα , followed by transfection with the same *mycer* construct as used in the instant application (i.e., c-myc cDNA construct fused to the ligand binding domain of an estrogen receptor; pg. 155 & 156; as it relates to claims 1a-c & 12a-c); thereby, establishing the clonal cell line, MNS-57. These MNS-57 cells were further cultured in the presence of a second mitogen, bFGF or EGF, in DF medium containing β-estradiol/ β-E2 (i.e., pgs. 155 & 157-159; Figs. 3 & 4; as it relates to claims 1d & 12d). However, Nakafuka et al. do not teach initial culturing of these neural precursor cells in medium that is serum-free, nor a method producing human neural precursor cells.

Weiss et al. teach that "a preferred embodiment for proliferation of neural stem cells is to use a defined serum-free culture medium, as serum tends to induce differentiation and contains unknown components" (col. 16, lines 23-26; as it relates to claims 1a & 12a). "The culture medium is supplemented with at least one proliferation-inducing growth factor" (col. 16, lines 41-42), in which "[p]referred proliferation-inducing growth factors include EGF and TGFα" (col. 16, lines 56-57; as it relates to claims 1b & 12b). Weiss also teach use of human pluripotent embryonic stem cells (cols. 13 & 15-16; as it relates to claims 4-5 & 15-16).

However, Weiss et al. do not disclose transfection of neural precursor/stem cells with c-myc constructs fused to steroid/thyroid hormone receptor ligand binding domains to form stable cell lines.

It would have been obvious to one of ordinary skill in the art at the time of filing Applicants' invention to modify Nakafuka's method of producing mammalian neural precursor/stem cells by using serum-free medium and culturing neural precursor cells in the presence of the first mitogen, EGF or TGFα, as taught by Weiss, in order to prevent premature differentiation of these neural precursor cells (which include Weiss' human pluripotent embryonic stem cells; as it relates to claims 4-5 & 15-16) prior to being transfected with Nakafuka's c-myc construct fused with the ligand binding domain of an estrogen receptor, which results in immortalization of these cells. Nakafuka's step (d) can subsequently be carried out using the second mitogens, aFGF or bFGF, along with β-estrodiol/ β-E2, to more accurately determine the effects of these defined components on the differentiation potential to neuronal-restricted cells, or alteratively to glial-restricted cells, etc.

7. Claims 1, 4-5, 12 & 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakafuka et al (IDS Ref #26), in view of Weiss et al. (U.S. Patent 5,851,832; IDS Ref #2) as applied to claims 1, 4-5, 12 & 15-16 above, and further in view of Eilers et al (IDS Ref #20) and/or Evans et al (1988).

Nakafuka et al. and Weiss et al. are as described above. However, neither Nakafuka et al. nor Weiss et al. teach use of Nakafuka's c-myc constructs fused to other steroid/thyroid hormone receptor ligand binding domains.

Eilers et al. teach that a "similar chimaera, *mycgr*, that contains the sequence that encodes the hormone [ligand] -binding domain of the rat glucocorticoid receptor fused to the 3' end of *myc* transforms these cells in a glucocorticoid-dependent manner (pg. 67, 1st *pp*; as it relates to claims 1 & 12).

Evans is a review describing the well known ligand binding domains of steroid/thyroid hormone receptors (e.g., pg. 891; as it relates to estrogen, androgen, progesterone, glucocorticoid, thyroid hormone, retinoid and ecdysone receptors and their respective ligands/myc-activating chemicals in claims 1c-d & 12c-d).

It would have been obvious to one of ordinary skill in the art to produce stable mammalian/human neural precursor cells using the method of Nakafuka et al. in view of Weiss et al. modified using any well known steroid/thyroid hormone receptor ligand binding domain fused to Eilers' c-myc constructs, because Eilers et al teach that "similar chimaeras" transform cells in a steroid/thyroid hormone-dependent manner.

8. Applicant's amendment and submission of an information disclosure statement under 37 CFR 1.97© with the fee set forth in 37 CFR 1.17(p) on 11/14/01 prompted the new ground(s) of rejection presented in this Office action.. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and § 609(B)(2)(I). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RCH

Robert C. Hayes, Ph.D.
April 11, 2002

Gary L. Kunz

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